

IN THE CLAIMS

This listing of the claims replaces all prior versions of the claims in the application.

1-11. (canceled)

12. (currently amended): A method of treating a subject for a breast cancer characterized by overexpression of the HER2 receptor protein, said method comprising concurrent therapy with an anti-HER2 antibody or fragment thereof that has anti-tumor activity and an interleukin-2 (IL-2) polypeptide comprising the sequence of SEQ ID NO:1 or biologically active variant thereof, wherein said anti-HER2 antibody or fragment thereof binds the same epitope as an anti-HER2 antibody selected from the group consisting of 4D5 and 520C9, wherein said concurrent therapy comprises administering to said subject at least one therapeutically effective dose of said IL-2 or variant thereof in combination with a dosing regimen for said anti-HER2 antibody or fragment thereof, wherein said dosing regimen for said anti-HER2 antibody or fragment thereof comprises administering to said subject at least one therapeutically effective dose of said anti-HER2 antibody or fragment thereof, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.5 MIU/m² to about 4.0 MIU/m²; wherein said variant of said IL-2 ~~activates NK cells~~ has anti-tumor activity and comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4, and wherein said anti-HER2 antibody or fragment thereof binds to the extracellular domain of the HER2 receptor protein.

13. (previously presented): The method of claim 12, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 2.0 mg/kg to about 9.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.6 MIU/m² to about 3.0 MIU/m².

14. (previously presented): The method of claim 13, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 3.0 mg/kg to about 8.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.8 MIU/m² to about 1.5 MIU/m².

15. (previously presented): The method of claim 14, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is about 4.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is about 1.0 MIU/m².

16. (currently amended): A method of treating a subject for a breast cancer characterized by overexpression of the HER2 receptor protein, said method comprising concurrent therapy with an anti-HER2 antibody or fragment thereof that has anti-tumor activity and an interleukin-2 (IL-2) polypeptide comprising the sequence of SEQ ID NO:1 or biologically active variant thereof, wherein said anti-HER2 antibody or fragment thereof binds the same epitope as an anti-HER2 antibody selected from the group consisting of 4D5 and 520C9, wherein said concurrent therapy comprises a first administration of a therapeutically effective dose of said IL-2 or variant thereof on day 1 of a treatment period followed by a first administration of a therapeutically effective dose of said anti-HER2 antibody or fragment thereof within 6 days of said first administration of said therapeutically effective dose of said IL-2 or variant thereof to said subject, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.5 MIU/m² to about 4.0 MIU/m²; wherein said variant of said IL-2 ~~activates NK cells~~ has anti-tumor activity and comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4, and wherein said anti-HER2 antibody or fragment thereof binds to the extracellular domain of the HER2 receptor protein.

17. (currently amended): A method of treating a subject for a breast cancer characterized by overexpression of the HER2 receptor protein, said method comprising concurrent therapy

with an anti-HER2 antibody or fragment thereof that has anti-tumor activity and an interleukin-2 (IL-2) polypeptide comprising the sequence of SEQ ID NO:1 or biologically active variant thereof, wherein said anti-HER2 antibody or fragment thereof binds the same epitope as an anti-HER2 antibody selected from the group consisting of 4D5 and 520C9, wherein said concurrent therapy comprises multiple dosing of a therapeutically effective dose of said anti-HER2 antibody or fragment thereof and a therapeutically effective dose of said IL-2 or variant thereof, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.5 MIU/m² to about 4.0 MIU/m²; wherein said variant of said IL-2 ~~activates NK cells~~ has anti-tumor activity and comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4, and wherein said anti-HER2 antibody or fragment thereof binds to the extracellular domain of the HER2 receptor protein.

18. (previously presented): The method of claim 17, wherein said multiple dosing comprises administering to said subject said therapeutically effective dose of said IL-2 or variant thereof and said therapeutically effective dose of said anti-HER2 antibody or fragment thereof during an introductory cycle, wherein said introductory cycle comprises daily administration of said therapeutically effective dose of said IL-2 or variant thereof on day 1 of said introductory cycle through day 20 of said introductory cycle, and a single administration of said therapeutically effective dose of said anti-HER2 antibody or fragment thereof on day 7 of said introductory cycle.

19. (previously presented): The method of claim 18, further comprising administering said therapeutically effective dose of said IL-2 or variant thereof and said therapeutically effective dose of said anti-HER2 antibody or fragment thereof during at least one subsequent cycle, wherein said subsequent cycle comprises daily administration of said therapeutically effective dose of said IL-2 or variant thereof on day 1 of said subsequent cycle through day 14 of

said subsequent cycle, and administration of said therapeutically effective dose of said anti-HER2 antibody or fragment thereof on day 1 of said subsequent cycle.

20. (previously presented): The method of claim 18, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 or variant thereof an intermediate dose of said IL-2 or variant thereof, wherein said intermediate dose is about 12.0 MIU/m².

21. (previously presented): The method of claim 19, further comprising intermediate-dose IL-2 pulsing on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 or variant thereof an intermediate dose of said IL-2 or variant thereof, wherein said intermediate dose is about 12.0 MIU/m².

22. (previously presented): The method of claim 12, wherein said IL-2 or variant thereof is administered subcutaneously.

23. (previously presented): The method of claim 12, wherein said anti-HER2 antibody comprises at least one human constant region.

24. (previously presented): The method of claim 12, wherein said anti-HER2 antibody is selected from the group consisting of a humanized anti-HER2 antibody, a chimeric anti-HER2 antibody, or a human anti-HER2 antibody.

25. (previously presented): The method of claim 12, wherein said anti-HER2 antibody is a humanized or chimeric form of a murine antibody selected from the group consisting of 4D5 and 520C9.

26. (previously presented): The method of claim 12, wherein said therapeutically effective dose of said IL-2 or variant thereof is administered as a pharmaceutical composition selected from the group consisting of a monomeric IL-2 pharmaceutical composition, a multimeric pharmaceutical IL-2 composition, a lyophilized IL-2 pharmaceutical composition, and a spray-dried IL-2 pharmaceutical composition.

27. (previously presented): The method of claim 26, wherein said IL-2 or variant thereof is recombinantly produced.

28. (currently amended): The method of claim 27, wherein said variant of ~~human IL-2~~ is des-alanyl-1, serine-125 human interleukin-2.

29. (previously presented): The method of claim 28, wherein said anti-HER2 antibody or fragment thereof comprises at least one human constant region.

30. (previously presented): The method of claim 28, wherein said anti-HER2 antibody is selected from the group consisting of a humanized anti-HER2 antibody, a chimeric anti-HER2 antibody, or a human anti-HER2 antibody.

31. (previously presented): The method of claim 28, wherein said anti-HER2 antibody is a humanized or chimeric form of a murine antibody selected from the group consisting of 4D5 and 520C9.

32. (previously presented): The method of claim 16, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 2.0 mg/kg to about 9.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.6 MIU/m² to about 3.0 MIU/m².

33. (previously presented): The method of claim 32, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 3.0

mg/kg to about 8.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.8 MIU/m² to about 1.5 MIU/m².

34. (previously presented): The method of claim 33, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is about 4.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is about 1.0 MIU/m².

35. (previously presented): The method of claim 17, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 2.0 mg/kg to about 9.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.6 MIU/m² to about 3.0 MIU/m².

36. (previously presented): The method of claim 35, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 3.0 mg/kg to about 8.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.8 MIU/m² to about 1.5 MIU/m².

37. (previously presented): The method of claim 36, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is about 4.0 mg/m² and wherein said therapeutically effective dose of said IL-2 or variant thereof is about 1.0 MIU/m².

38. (previously presented): The method of claim 18, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 2.0 mg/kg to about 9.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.6 MIU/m² to about 3.0 MIU/m².

39. (previously presented): The method of claim 38, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 3.0 mg/kg to about 8.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.8 MIU/m² to about 1.5 MIU/m².

40. (previously presented): The method of claim 39, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is about 4.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is about 1.0 MIU/m².

41. (previously presented): The method of claim 19, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle and on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 or variant thereof an intermediate dose of said IL-2 or variant thereof, wherein said intermediate dose is about 12.0 MIU/m².

42. (currently amended): A method of treating a subject for a breast cancer characterized by overexpression of the HER2 receptor protein, said method comprising concurrent therapy with an anti-HER2 antibody or fragment thereof that has anti-tumor activity and an interleukin-2 (IL-2) polypeptide comprising the sequence of SEQ ID NO:1 or biologically active variant thereof, wherein said anti-HER2 antibody or fragment thereof binds the same epitope as an anti-HER2 antibody selected from the group consisting of 4D5 and 520C9, wherein said concurrent therapy comprises daily administration of a therapeutically effective dose of said IL-2 or variant thereof on day 1 of an introductory cycle through day 20 of said introductory cycle, and a single administration of a therapeutically effective dose of said anti-HER2 antibody or fragment thereof on day 7 of said introductory cycle; wherein said variant of said IL-2 ~~activates NK cells~~ has anti-tumor activity and comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4, and wherein said anti-HER2 antibody or fragment thereof binds to the extracellular domain of the HER2 receptor protein.

43. (previously presented): The method of claim 42, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or biologically active variant thereof is in the range from about 0.5 MIU/m² to about 4.0 MIU/m².

44. (previously presented): The method of claim 43, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 2.0 mg/kg to about 9.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.6 MIU/m² to about 3.0 MIU/m².

45. (previously presented): The method of claim 44, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is in the range from about 3.0 mg/kg to about 8.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is in the range from about 0.8 MIU/m² to about 1.5 MIU/m².

46. (previously presented): The method of claim 45, wherein said therapeutically effective dose of said anti-HER2 antibody or fragment thereof is about 4.0 mg/kg and wherein said therapeutically effective dose of said IL-2 or variant thereof is about 1.0 MIU/m².

47. (previously presented): The method of claim 42, further comprising administering said therapeutically effective dose of said IL-2 or variant thereof and said therapeutically effective dose of said anti-HER2 antibody or fragment thereof during at least one subsequent cycle, wherein said subsequent cycle comprises daily administration of said therapeutically effective dose of said IL-2 or variant thereof on day 1 of said subsequent cycle through day 14 of said subsequent cycle, and administration of said therapeutically effective dose of said anti-HER2 antibody on day 1 of said subsequent cycle.

48. (previously presented): The method of claim 42, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 or variant thereof an intermediate dose of said IL-2 or variant thereof, wherein said intermediate dose is about 12.0 MIU/m².

49. (previously presented): The method of claim 47, further comprising intermediate-dose IL-2 pulsing on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 or variant thereof an intermediate dose of said IL-2 or variant thereof, wherein said intermediate dose is about 12.0 MIU/m².

50. (previously presented): The method of claim 47, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle and on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 or variant thereof an intermediate dose of said IL-2 or variant thereof, wherein said intermediate dose is about 12.0 MIU/m².

51. (canceled)

52. (currently amended): The method of claim ~~54~~ 12, wherein said anti-HER2 antibody is a humanized form of a murine antibody selected from the group consisting of 4D5 and 520C9.

53. (previously presented): The method of claim 52, wherein said IL-2 or variant thereof is recombinantly produced.

54. (canceled)

55. (currently amended): The method of claim ~~54~~ 16, wherein said anti-HER2 antibody is a humanized form of a murine antibody selected from the group consisting of 4D5 and 520C9.

56. (previously presented): The method of claim 55, wherein said IL-2 or variant thereof is recombinantly produced.

57. (canceled)

58. (currently amended): The method of claim ~~57~~ 17, wherein said anti-HER2 antibody is a humanized form of a murine antibody selected from the group consisting of 4D5 and 520C9.

59. (previously presented): The method of claim 58, wherein said IL-2 or variant thereof is recombinantly produced.

60. (canceled): The method of claim 42, wherein said cancer is breast cancer.

61. (currently amended): The method of claim ~~60~~ 42, wherein said anti-HER2 antibody is a humanized form of a murine antibody selected from the group consisting of 4D5 and 520C9.

62. (previously presented): The method of claim 61, wherein said IL-2 or variant thereof is recombinantly produced.

63. (currently amended): A method of treating a subject for a breast cancer characterized by overexpression of the HER2 receptor protein, said method comprising concurrent therapy with an IL-2 polypeptide comprising the amino acid sequence of SEQ ID NO:1 and a humanized anti-HER2 antibody selected from the group consisting of a humanized 4D5 antibody and a humanized 520C9 antibody, wherein said concurrent therapy comprises administering to said subject at least one therapeutically effective dose of said IL-2 polypeptide in combination with a dosing regimen for said humanized anti-HER2 antibody, wherein said dosing regimen for said humanized anti-HER2 antibody comprises administering to said subject at least one therapeutically effective dose of said humanized anti-HER2 antibody, wherein said therapeutically effective dose of said humanized anti-HER2 antibody is in the range from about 1.0 mg/kg to about 10.0 mg/kg and wherein said therapeutically effective dose of said IL-2 polypeptide is in the range from about 0.5 MIU/m² to about 4.0 MIU/m².

64. (previously presented): The method of claim 63, wherein said anti-HER2 antibody is a humanized 4D5 antibody.

65. (previously presented): The method of claim 63, wherein said anti-HER2 antibody is a humanized 520C9 antibody.

66. (previously presented): The method of claim 63, wherein said therapeutically effective dose of said humanized anti-HER2 antibody is about 4.0 mg/kg and wherein said therapeutically effective dose of said IL-2 polypeptide is about 1.0 MIU/m².

67. (previously presented): The method of claim 63, wherein said concurrent therapy comprises a first administration of a therapeutically effective dose of said IL-2 polypeptide on day 1 of a treatment period followed by a first administration of a therapeutically effective dose of said humanized anti-HER2 antibody or fragment thereof within 6 days of said first administration of said therapeutically effective dose of said IL-2 polypeptide to said subject.

68. (previously presented): The method of claim 63, wherein said concurrent therapy comprises multiple dosing of a therapeutically effective dose of said humanized anti-HER2 antibody and a therapeutically effective dose of said IL-2 polypeptide.

69. (previously presented): The method of claim 68, wherein said multiple dosing comprises administering to said subject said therapeutically effective dose of IL-2 polypeptide and said therapeutically effective dose of said humanized anti-HER2 antibody during an introductory cycle, wherein said introductory cycle comprises daily administration of said therapeutically effective dose of said IL-2 polypeptide on day 1 of said introductory cycle through day 20 of said introductory cycle, and a single administration of said therapeutically effective dose of said humanized anti-HER2 antibody on day 7 of said introductory cycle.

70. (previously presented): The method of claim 63, further comprising administering said therapeutically effective dose of said IL-2 polypeptide and said therapeutically effective dose of said humanized anti-HER2 antibody during at least one subsequent cycle, wherein said subsequent cycle comprises daily administration of said therapeutically effective dose of said IL-2 polypeptide on day 1 of said subsequent cycle through day 14 of said subsequent cycle, and

administration of said therapeutically effective dose of said humanized anti-HER2 antibody on day 1 of said subsequent cycle.

71. (currently amended): The method of claim ~~63~~ 69, further comprising intermediate-dose IL-2 pulsing on days 8-10 of said introductory cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 polypeptide an intermediate dose of said IL-2 polypeptide, wherein said intermediate dose is about 12.0 MIU/m².

72. (currently amended): The method of claim ~~63~~ 70, further comprising intermediate-dose IL-2 pulsing on days 1-3 of said subsequent cycle, wherein said pulsing comprises administering in place of said therapeutically effective dose of said IL-2 polypeptide an intermediate dose of said IL-2 polypeptide, wherein said intermediate dose is about 12.0 MIU/m².

73. (previously presented): The method of claim 63, wherein said IL-2 polypeptide is administered subcutaneously.

74. (new): The method of claim 31, wherein said anti-HER2 antibody is Herceptin®.

75. (new): The method of claim 52, wherein said anti-HER2 antibody is Herceptin®.

76. (new): The method of claim 55, wherein said anti-HER2 antibody is Herceptin®.

77. (new): The method of claim 58, wherein said anti-HER2 antibody is Herceptin®.

78. (new): The method of claim 61, wherein said anti-HER2 antibody is Herceptin®.

79. (new): The method of claim 63, wherein said anti-HER2 antibody is Herceptin®.